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TITLE: The Effect of COX-2 Inhibitors on the Aromatase Gene (CYP19) Expression in Human Breast Cancer

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13. ABSTRACT ***(Maximum 200 Words)***

Aromatase (CYP-19) is responsible for estrogen biosynthesis within breast tumor tissue. Aromatase and cyclooxygenase-2 (COX-2) are both overexpressed in human breast cancer, and increased levels of prostaglandin (PG) activates the CYP19 promotor and increases gene expression. We hypothesize that celecoxib, a selective COX-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. To test this hypothesis, in DOD grant # DAMD17-01-1-0589, tumor tissue will be collected from breast cancer patients at the initial diagnosis, and again at the definitive surgery (lumpectomy or mastectomy) for breast cancer. In the 10-14 day interval before the definitive surgery, patients will receive celecoxib and tissue samples collected before and after treatment with celecoxib will be evaluated for gene expression of COX-2 and CYP19. If our hypothesis is correct, then expression of the CYP19 gene will decrease in response to celecoxib. This study will provide preliminary data to a) support a mechanism whereby COX-2 inhibitors decrease estrogen production within breast tumors by decreasing CYP19 expression; and b) provide the rationale for initiating larger chemoprevention and therapeutic trials of COX-2 inhibitors in high risk and breast cancer patients.

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breast cancer

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INTRODUCTION

This study will test the hypothesis that celecoxib, a selective Cox-2 inhibitor, will decrease PG, decrease the expression of CYP19, and reduce estrogen biosynthesis within tumor tissue. The primary objective of the study is to evaluate Aromatase (CYP19) and estrogen receptor (ER) gene expression by reverse-transcriptase polymerase chain reaction (RT-PCR) in response to a selective cyclooxgenase-2 (COX-2) inhibitor, celecoxib, in paired tumor tissue collected at the time of the initial diagnosis and at the time of definitive surgery for localized, non-metastatic breast cancer patients. The secondary objective is to evaluate the effect of celecoxib on the following biomarkers: estrogen receptor, progesterone receptor, Her-2/neu, Ki-67, COX-1, COX-2, CYP19, CD31, and PGE2, and Aromatase activity in paired tissue specimens by standard immunohistochemical methods. The study is approved by The Ohio State University IRB; however, is pending Army approval. In total, 34 subjects will be enrolled on the study. We anticipate that approximately 15 of the 34 subjects will be enrolled during the first year of the study.

BODY

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

KEY RESEARCH ACCOMPLISHMENTS

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

REPORTABLE OUTCOMES

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

CONCLUSIONS

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

REFERENCES

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.

APPENDICES

Not applicable. The study has not yet been opened to accrual at The Ohio State University. Army approval is pending.